



2023 CALERIE™ PILOT GRANT APPLICATION INSTRUCTIONS

Purpose:

The CALERIE™ Network, supported by NIA (R33AG070455), invites applications proposing ancillary and pilot projects using CALERIE trial data and biosamples. Approximately \$90,000 in total direct costs is available to fund approximately three projects, depending on merit, during FY 2024. The major objective of this program is to **expand the diversity and number of investigators in aging biology and grow a network of researchers interested in caloric restriction**. Ideally, recipients of this award will use this support to generate preliminary data for successful applications for extramural research funding (e.g., NIH R01, potentially targeting [NOT-AG-23-024](#) - Notice of Special Interest (NOSI): Analyses of CALERIE Datasets and Biospecimens to Elucidate the Biological Effects and the Behavioral and Psychological Aspects of Sustained Caloric Restriction in Humans).

This program encourages:

- Early career investigators to develop the needed preliminary data to support new grant applications;
- Established investigators to mentor younger investigators in using novel approaches and techniques in support of application for new funding;
- Formation of multidisciplinary research teams including behavioral, clinical, molecular and biostatistical expertise.

We especially encourage applications from early-stage investigators from under-represented backgrounds, as well as investigators from different fields who bring novel approaches that enhance our understanding of how caloric restriction affects human health and life span. We encourage all early-stage investigators to apply as a PI and to collaborate with a more senior mentor with expertise in translational research.

Typically, funding is provided for a one-year period from the date of award. In special circumstances and with adequate justification, there may be allowances for a no-cost extension.

Note that facilities and administrative costs for CALERIE™ Pilot grants will be included in the total award; when developing budgets, investigators should consider their institutional F&A costs.

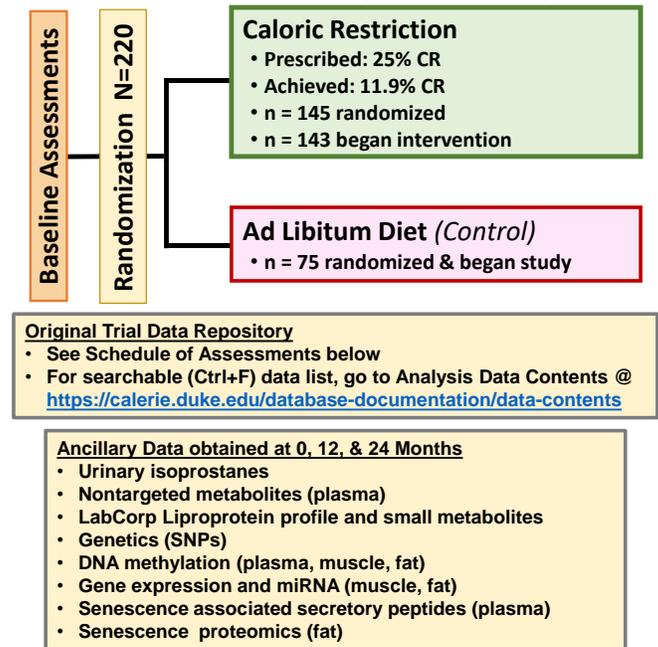
Who is Eligible?

Post-doctoral fellows, Graduate Medical Residents/Fellows, Assistant Professors, and Associate Professors from US and Canadian universities, colleges, medical schools, and similar training programs. Applications from other international institutions will not be considered. *Applicants must hold a PhD, MD, or equivalent degree.*

- Early-stage investigators who do not have current or previous NIH (or equivalent) independent research support (excluding fellowship or career development awards)
- Teams comprised of an early-stage investigator (junior faculty or senior postdoc) and senior faculty (senior as mentor only) working together to tackle a question of high priority to the CALERIE™ Network.

- Collaborative teams of behavioral, clinical, molecular and biostatistical investigators working together to develop translational studies pursuing questions of high priority to the CALERIE™ Network. **Collaborative projects with multiple areas of expertise are strongly encouraged.**
- Projects using CALERIE™ data for systems biology to explain the observed beneficial effects of calorie restriction on lifespan, health span, and intermediate surrogates will be reviewed favorably.
- For investigators who have previously received CALERIE™ Network Pilot funding, review will place greater emphasis on the novelty of the newly proposed study and the plan for independent funding.
- There is no citizenship requirement, but applications should have documented institutional support and a faculty or postdoctoral position for the duration of the project.

Figure 1: CALERIE Design and Sample and Data Repository



More about CALERIE™:

The Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE™) was a randomized controlled trial designed to assess the effects in humans of two years of sustained caloric restriction (CR) without a specific macronutrient composition. The overall objective was to elucidate underlying biological mechanisms and mediators of primary and secondary aging in humans. Providing a rich resource for ancillary and pilot projects, the rigorous design and execution of the CALERIE™ intervention produced comprehensive phenotypic data coupled to biological samples.

Participants were healthy-weight to mildly overweight adults in early to mid-adulthood ($22.0 \leq \text{BMI} < 28 \text{ kg/m}^2$; ages 21-50 years). Participants ($n=220$) were randomized in a 2:1 ratio to a 2-year intervention designed to achieve 25% CR or an *ad libitum* (AL) diet. Assessments were performed at baseline, 3, 6, 12, 18 and 24 months. One can think of the CALERIE™ intervention in two components based on physiological and behavioral responses to CR—a weight loss period lasting approximately one year, and a weight maintenance period during the second year of the intervention. An average of ~12% CR was achieved during the 2-year intervention, with retention of ~85% of participants. With respect to cardiometabolic outcomes, there were two main types of responses: 1) an initial improvement in the CR group relative to AL in the first

Evaluation	Study Month										
	Baseline	1	3	6	9	12	17	18	23	24	
Inpatient GCRC Visits											
Calorie Restricted Group	XX			XX		XX		X		XX	
Control Group	XX			XX		XX				XX	
General Examinations											
Medical and medication history	X										
Physical Exam	X					X				X	
Vital Signs	X	X	X	X	X	X	X	X	X	X	
Medications	X	X	X	X	X	X		X		X	
Electrocardiogram (ECG)	X	X	X	X	X	X		X		X	
Adverse Events	X	X	X	X	X	X		X		X	
Safety Assessments											
Hematology & Serum Chemistry	X	X	X	X	X	X		X		X	
Urinalysis	X	X	X	X	X	X		X		X	
Pregnancy Test (Females only)	X			X*		X	X	X*	X	X	
Body Weight, Body Composition & Bone Assessments											
Clinic Weights	X	X	X	X	X	X	X	X	X	X	
Home Weights	XX			X		X		X		X	
Waist Circumference	X	X	X	X	X	X		X		X	
Fat Mass / Fat-Free Mass (DXA)	XX			XX*		X		X*		X	
Markers of bone formation/resorption	X			X		X				X	
Metabolic Assessments											
Total Energy Expenditure by DLW	XX			X*		X		X*		X	
Resting Metabolic Rate (RMR)	XX			X*		X		X*		X	
Core Temperature	X			X		X				X	
Cardiovascular & Endocrine Assessments											
Blood Pressure	X	X	X	X	X	X	X	X	X	X	
Oral Glucose Tolerance Test (OGTT)	X					X				X	
Bloodwork	X					X				X	
Immune Function											
Delayed-type hypersensitivity (DTH)	X					X				X	
Antibody response to vaccines	X						X	X	X	X	
Questionnaires											
4 Psychological Questionnaires	X			X		X				X	
Cognitive Assessment	X			X		X				X	
7-Day Physical Activity Recall	X XX X			XX*		XX		XX*		XX	
Muscle Strength and Endurance											
Isokinetic Strength	X					X		X		X	
Grip Strength	X					X		X		X	
VO ₂ max	X					X		X		X	
Archival Specimens											
Blood (WBC, serum & plasma)	X		X	X		X		X		X	
Urine (24-hour collection)	X					X				X	
Muscle (quadriceps biopsy) -	X					X				X	
Fat (abdominal biopsy) - optional	X					X				X	

* Calorie Restricted group only

year (during weight loss), with maintenance of cardiometabolic improvements during the second year (weight maintenance) or 2) minimal improvement as compared to AL in the first year (during weight loss), followed by significant improvement in the second year (during weight maintenance).

This remarkable observation implies that there exists some unique biology underlying sustained CR beyond one year with respect to these outcomes. As they represent a difference between the weight loss and the weight maintenance phases of calorie restriction biology, developing a better understanding of biology of these two types of time-course responses is a major goal for this funding opportunity. A schematic of the CALERIE design, assessments, and available data and samples is shown in Figure 1. Please see www.CALERIE.duke.edu for additional information about the CALERIE™ trial design, publications, sample types, collection details (manual of procedures), and available data.

Application Details: (See Instructions below)

Letter of Intent (LOI)*

Revised Deadline: 1 November 2023

To: annsley.winders@duke.edu

Invitation to present to the CALERIE Research Network Steering Committee**

By invitation

Invitation Notification: ~ 1 December 2023

Presentation: ~ 15 December 2023

Full Application†

Due: 5 January 2024

To: https://calerie.duke.edu/apply_pilot_study

Funding Decisions‡

By 1 February 2024

Funding Available

By 1 April-May 2024

***Letter of Intent Guidelines:**

A letter of intent is required initially to ensure eligibility and appropriateness of the research topic and to provide a rough estimate of the budget (note: awards will be made on the basis of total costs, including F&A). Documents for the LOI and full application should be submitted as ONE DOCUMENT electronically (PDF format in color).

- One page maximum
- Project title, Principal Investigator and, if applicable, inter-institutional collaborations.
- General description of intended work, including requests for CALERIE™ data, samples (include types and amounts), and statistical assistance from the CALERIE™ Research Network statistical team.
- Estimated budget.
- If applicable, name of collaborative mentor.
- A strong Letter of Support from the applicant's Program Director, Division Chief, or Department Chair.
- For applicants in postdoctoral positions or nearing program completion, the Letter of Support should document institutional commitment for the duration of the project.
- NIH Biosketch.

****Invited Presentation Guidelines:**

Selected investigators will be invited to give a 15-minute presentation on the following to the CALERIE™ Research Network/Selection Committee:

Significance

- Does the project address an important problem or a critical barrier to progress in the field?
- If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved?
- How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Innovation

- Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions?

Investigator

- Are the PI(s), collaborators, and mentors well suited to the project? Does the investigator have the methodologic expertise or collaborators with expertise to perform the project?

Approach

- Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project?
- Scientific rigor: are the planned study design, methods and statistical approaches likely to generate high-quality data worthy of publication or for use as preliminary data in a future grant application?

Feasibility

- Is the estimated budget sufficient to cover all project costs? If not, what other support is promised?
- Is the research feasible within the allotted time frame?

† Full Application Guidelines:

Only investigators receiving approval following their presentation will be eligible to submit a full application.

Format of Application: The application packet must include the following (Applicants are required to use the NIH 398 forms):

- NIH Face Page (Please include signature of institution official confirming acknowledgement of a waiver for F&A costs)
- NIH Budget page + 1 page budget justification
- NIH Biographical Sketch including "Other support" if currently independently funded.
- NIH Biographical Sketch from the mentor if applicable
- Research plan (**5-page maximum including references, Arial 11, single-spaced, 0.5-inch margins**).

The following headings should be used for the research plan.

- A. Specific Aims:** State concisely the hypothesis to be tested and the specific aim(s) to be achieved during the grant period. The aims must be reasonable to achieve during the one-year period of the grant.
- B. Significance and Innovation:** State the relevance of the proposed project to aging biology and highlight technical or conceptual innovative features.
- C. Research Design and Methods:** Discuss your relevant prior work that will help to establish the experience and competence of your project. Concisely present your project rationale, experimental design and the methods to accomplish your specific aims. Indicate how the results will be interpreted and how they will lead to future investigations. Well-known methods and standard procedures may be described very briefly or referenced, but novel experimental approaches should be outlined in more detail. This section should represent the bulk of the application. If relevant, discuss the role of the mentor and collaborators in the design and execution of the proposed research
- D. Requests for data and samples, including sample type (i.e., blood, muscle, adipose), time point (i.e., 0, 3, 6, 9, 12, 18, 24 months), and numbers.**
- E. Description of how the results of this study will lead to future investigations/grant applications.** Confirmation that data will be returned to the CALERIE™ data repository within six months of data finalization.
- F. References:**
- G. Appendix :**
 - Letters of support

Additional Instructions:

1. Please list the Principal Investigator's (PI) name on the top right-hand corner of every page of the application.
2. When completing the budget page, please refer to the list below of Expenditures Allowed and Expenditures NOT Allowed (see below).
3. Although facilities and administrative costs are allowed under the terms of the prime award, it is our belief that these funds should be used in the spirit intended (i.e., direct costs in support of this

project). **It is hoped that for an award of this type, your institution will be willing to forego the facilities and administrative costs and consider these costs as matching funds to your project.**

4. If project involves a sponsor, a consultant, or a mentor, this individual must write a letter of support for the application and clarify any potential overlap between their support and the subject of the proposal.

‡Chosen awards will require approval of the NIA, issuance of funds to the CALERIE™ Research Network, before awards can be contracted with the investigators' institutions.

Allocation and Expenditure of Funds:

Expenditures Allowed:

- Limited technical staff salary support (do not request more than 25% salary for a research associate)
- Research supplies
- Equipment costing less than \$5,000.
- Special fees (pathology, photography, etc.)
- Costs for sample shipment

Expenditures NOT Allowed:

- Principal Investigator, Co-Investigator, or Mentor salary support
- Secretarial/administrative personnel salary support
- Office equipment and supplies
- Computers
- Tuition
- Domestic or Foreign Travel
- Publication costs, including reprints
- Dues and membership fees in scientific societies
- Purchasing and binding of periodicals and books
- Honoraria and travel expenses for visiting lecturers
- Rental of office or laboratory space
- Construction or building maintenance
- Recruiting and relocation expense

Scoring metric:

Applications are scored using the NIH criteria for Significance (including scientific premise), innovation, approach (including scientific rigor, reproducibility and biological variables), investigator(s), and environment. Other score driving factors include likelihood of successful execution within the funding constraints (cost and time), potential for future funding, available mentoring and other Faculty/Institutional support.

Additional Information:

CALERIE™ data are de-identified. The Duke Clinical Research Institute will facilitate data and material transfer agreements in conjunction with the investigator's institution and coordinate necessary Duke IRB amendments. Investigator IRB submissions should occur when the full application is submitted for review. IRB approval will be requested as per the NIH practice of just-in-time mechanism before funding is released.

For more information: Please check our CALERIE™ website <http://calerie.duke.edu>

Application questions: Kim Huffman: kim.huffman@duke.edu MPI, General queries

Annley Winders: annsley.winders@duke.edu Project Director, DCRI; LOI receipt

Consultations regarding CALERIE design or study design, your project relevance to NIA, or available statistical support: Chhanda Dutta; duttac@nia.nih.gov: NIA relevance and logistical questions

Corby Martin Corby.Martin@pbrc.edu: Behavioral study queries

Bill Kraus William.Kraus@duke.edu: Molecular/Integrative study queries

Carl Pieper Carl.Pieper@duke.edu: Statistical queries